Clinical Experience With Permanent Mechanical Circulatory Assistance

By ADRIAN KANTROWITZ, JACQUES L. SHERMAN, JR., AND JOSEPH KRAKAUER

WITH CONCURRENT ADVANCES in surgical techniques, electronics technology, and materials, interest in mechanical methods of assisting the failing heart is accelerating. Our work during recent years has been primarily concerned with the development of a permanent intracorporeal auxiliary ventricle for continuous or intermittent use in the treatment of intractable left ventricular failure. Experimental evidence of hemodynamic effectiveness and biological tolerance to the device led to our first clinical implantations in 1966.

The genesis of the auxiliary ventricle was implicit in studies undertaken at Western Reserve University in 1951 when we sought to augment coronary flow by retardation of the arterial pressure pulse. These experiments suggested that out-of-phase perfusion might prove surgically feasible as a means of improving coronary flow.[1] Since then, numerous workers including Harken,[2,3,4] Watkins,[5] Soroff,[6,7] and Goldfarb[8,9] have applied this principle of counterpulsation in developing various methods of temporary circulatory support.

In our first attempt to develop a surgical method to assist the failing heart, the left hemidiaphragm was utilized as an auxiliary ventricle.[10,11] Although the use of autogenous muscle had advantages, the workload of the left ventricle was not sufficiently reduced for adequate support. We therefore turned to the development of a mechanical auxiliary ventricle which would lend effective hemodynamic support, cause minimal damage to the blood, and not interfere with the function of other organs. An intracorporeal device dictated construction of biologically compatible materials and a surgical procedure of tolerable risk.

An air-powered, bulb-shaped device of Silastic with woven Dacron cuffs was fabricated.[12] By implanting various sized bulbs at different sites in the abdominal and thoracic aortas, we found that the bulb's effectiveness was proportional to its proximity to the heart, with the greatest decrease in ventricular pressure in the aortic arch bypass position. To minimize bending stresses and maintain a smooth blood flow, an ellipsoidal-shaped unit was designed and tested.[13] A series of modifications led to our current U-shaped design (Fig. 1).

Acute and chronic hemodynamic studies with the U-shape functioning in normal dogs up to 104 days with 303 pumping hours showed a consistent 40–50 per cent reduction in left ventricular work and a 20 per cent increase in

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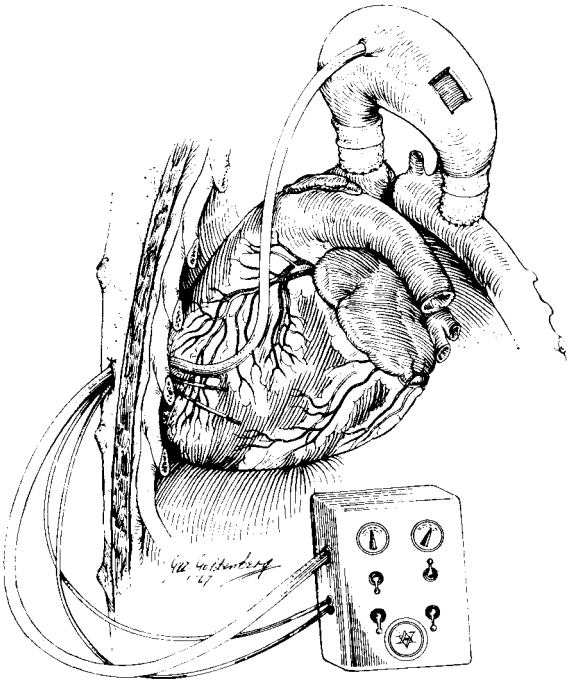

Fig. 1.—Kantrowitz-Avco mechanical auxiliary ventricle system: implanted pump connected to extracorporeal unit.

coronary flow.[14] The cardiac output was unchanged or slightly increased. Weekly studies with a functioning U-pump showed a fall in hemoglobin and RBC values during the first postoperative days, but these values generally returned to normal within two weeks. A series of acute experiments was undertaken to determine the hemodynamic effects of the auxiliary ventricle on dogs in induced congestive heart failure. The data confirmed our general findings with normal dogs, and improvements during failure were even more marked.[15]

Patency studies[16] with non-functioning U-shaped units showed very little trauma to the blood elements. Biopsy and autopsy reports on dogs surviving 4–6 months showed relatively slight tissue reactions to either polyurethane or Silastic bulbs on macroscopic examination. In animals with shorter survival times, a slight chronic granulomatous inflammation, which was more prominent around the Dacron cuffs than around the plastic housing, was observed. In those with longer survival times, more acellular collagenous tissue was found on histologic examination. The inner surface of the blood-handling chambers remained free of accretions as did the connecting points of the cuffs. The lungs were well expanded and partially adherent to the unit and cuffs, and other organs revealed no abnormalities attributable to the implanted ventricle; the implants were well tolerated.

Description of Current System

The system developed in collaboration with the Avco-Everett Research

Laboratory consists of a U-shaped pump (Fig. 1) of Silastic and an extracorporeal driving unit. The U-shaped unit, a flexible bulb inside a rigid plastic case, can be used for intermittent or continuous pumping. It is implanted 2 cm. from the aortic root, allowing for full lung expansion, and is connected by cuffs of Dacron arterial graft to the ascending and descending aorta, closely paralleling the aortic arch. The descending aorta is interrupted just above the proximal anastomosis, thus placing the mechanical ventricle in series with the anatomical ventricle. Two electrodes implanted in the myocardium of the left ventricle pick up the R wave of the electrocardiogram, which triggers the release of compressed air from the external power supply into the bulb.

When the mechanical auxiliary ventricle is operating, the flexible bulb is expanded during natural ventricular systole, thus providing a low pressure and resistive load during the systolic ejection phase (Fig. 2). Approximately 10 msec. after closure of the aortic valves, the bulb is contracted, forcing blood in the plastic ventricle retrograde against the closed aortic valve and into the coronary arteries, and forward into the descending aorta through the distal graft. The superimposition of mechanical systole on the pulse wave can be seen in Figure 3.

When the pump is not operating, the unit functions only as an obligatory shunt from the ascending to descending aorta. No artificial valves are needed since the patient's aortic valve and the pressure differentials establish the direction of blood flow.

In either mode of operation, satisfactory blood flow to the great arteries of the aortic arch is achieved by retrograde flow from the distal anastomosis up the descending aorta.

Clinical Application

As previously reported,[17] the U-shaped auxiliary ventricle was first implanted in a patient during February 1966. The candidate was a 33-year-old man with chronic left ventricular failure, alcoholic myocarditis, and severe cirrhosis of the liver. Chronic left ventricular failure of 3 year's duration was due to cardiomyopathy. Electrocardiogram and vectorcardiogram showed a pattern of left ventricular hypertrophy, intraventricular conduction disorder and diaphragmatic wall myocardial infarction. Cineangiocardiography showed that the left ventricle was dilated markedly and exhibited poor contractibility. On February 4, 1966, a mechanical auxiliary ventricle was implanted.

A tracheostomy was performed immediately postoperatively because of poor ventilation, and mechanical assistance was given to respiration. Although the early postoperative course was fairly stable, a marked diminution in platelet count and bleeding pointed to dysfunction of the diseased liver. The patient died 20 hours postoperatively because of decreased myocardial compliance secondary to the cardiomyopathy and uncontrollable tachycardia. This produced right ventricular failure, which became the limiting factor of cardiac output and on which synchronous diastolic augmentation of the left ventricle had little or no effect.

The second clinical implantation was performed in a 63-year-old woman, admitted in April 1966 to the Coney Island Hospital in severe, acute and

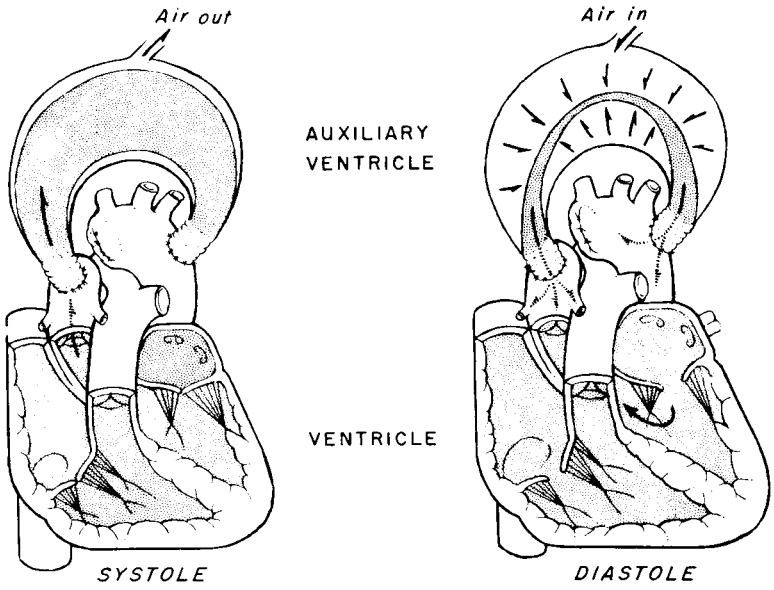

Fig. 2.—Functioning of auxiliary ventricle.

chronic congestive heart failure. She had suffered two episodes of myocardial infarction in 1959 and had been incapacitated since the second attack. Because of progressive congestive heart failure she had been bedridden for 3 years prior to admission despite therapy. Diabetes mellitus was diagnosed 7 years prior to her admission. Significant physical findings included BP 115/90, pulse rate 112 and regular respirations at 40 per min. Her occular fundi showed numerous microaneurysms and several retinal hemorrhages. Neck veins were distended at 90°, and there were moist rales and rhonchi in both lung fields. Her heart was enlarged and there was a diastolic gallop present, but no murmurs were audible. Massive peripheral edema involving the abdomen, back, and lower extremities made examination of these areas impossible. The ECG, chest x-ray, and laboratory studies confirmed the presence of an old anteroseptal myocardial infarction, congestive heart failure, cardiac enlargement, diabetes mellitus, acute and chronic pyelonephritis, slight elevation of plasma urea and impaired liver function consistent with cardiac cirrhosis.

Conventional therapy gave the patient some relief but failed to improve significantly the congestive heart failure. A regimen of ethacrynic acid and spironolactone therapy induced a massive diuresis over a 5-day period with a net loss of 21,355 cc. (approximately 47 lb.) of edema fluid. Her dry weight was readily maintained thereafter and the patient was greatly improved clinically. Additional examinations at this time demonstrated a slightly enlarged liver and the presence of severe diabetic neuropathy and muscle atrophy of the lower extremities.

She was transferred to Maimonides Hospital where right and left cardiac catheterization showed no valvular defects or shunts. Her cardiac index was

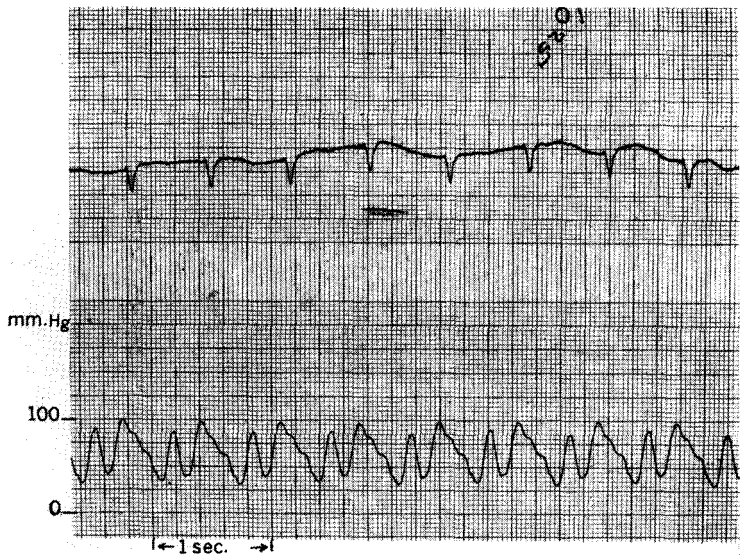

Fig. 3.—Electrocardiogram (top) and radial artery pressure curve (bottom) during operation of the mechanical auxiliary ventricle. Note that the wave generated by the mechanical ventricle at this particular setting has a higher peak than the natural systolic peak. The height of these peaks can be modified by adjustment of the stroke volume of the mechanical auxiliary ventricle.

1.8 L./min./m^2. Right ventricular end diastolic pressure and right atrial mean pressures were normal. Left ventricular end diastolic pressure and systemic and pulmonary resistances were all moderately elevated. These data were obtained at a time when the patient was hypovolemic with a plasma volume (Cr^{51}) of 29 ml./Kg. (vs. normal of 38).

Hematological evaluation showed reductions in prothrombin consumption, fibrinogen, and in factors II, V, VII, and X. Pulmonary function tests showed only a minimal degree of restrictive defect.

Surgical Procedure

On May 18, 1966, a mechanical auxiliary ventricle was implanted through an anterior transverse transsternal thoracotomy. Since the heart was enlarged and the thoracic cavity was relatively small, it was necessary to place the prosthesis in the posterior sulcus of the apex of the right hemithorax instead of the left.

After insertion of the mechanical ventricle the aorta was cross-clamped above the proximal anastomosis prior to the planned ligation. However, left ventricular pressure increased and brachial artery pressure decreased, making it impossible to transect the aorta. The lumen of the aorta was then narrowed by a Teflon band as much as possible without causing a perceptible rise in left ventricular pressure. The mechanical auxiliary ventricle operated satisfactorily with this modified circuit and the operation was completed. The patient withstood the operative procedure well.

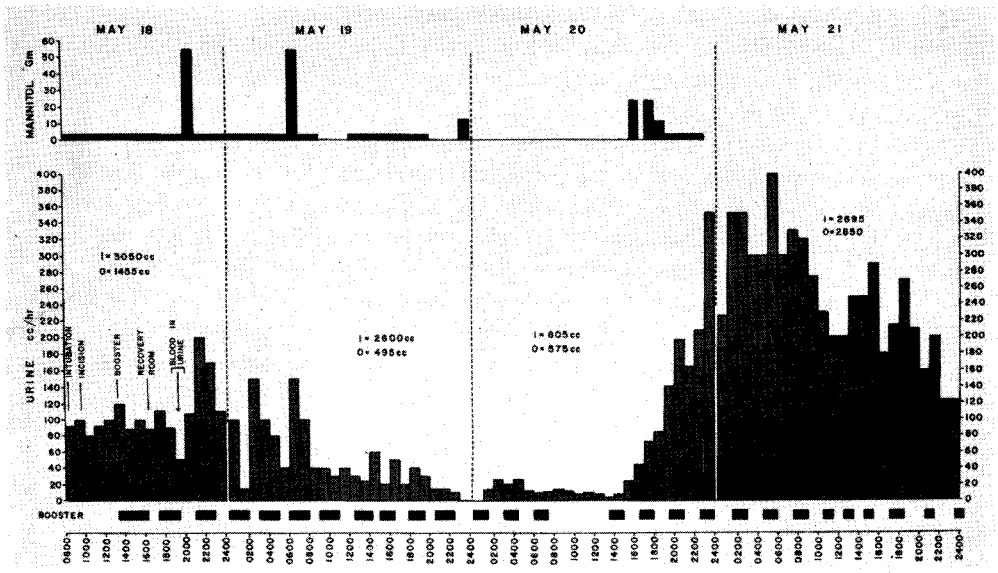

Fig. 4.—Urinary output and operating schedule of mechanical auxiliary ventricle. Ordinate of lower graph shows urinary output in cc./hour. Ordinate of upper portion shows amount of mannitol infusion. The time scale is shown in 2 hour intervals on the abscissa. Horizontal shaded blocks above time scale show periods of operation of mechanical auxiliary ventricle. Values of I and O represent total daily fluid intake and output in cc.

Postoperative Course

The mechanical auxiliary ventricle was in operation intermittently for varying periods of time although usually on for 2 hours and off for 1 hour (Fig. 4). The patient regained consciousness and had a relatively normal postanesthetic recovery.

Urinary output, which had been maintained at satisfactory levels throughout the operative period, began to decline and by the morning after surgery the patient was in frank, acute renal failure (Fig. 4) with oliguria and inability to achieve osmolar or urea concentration. On the following day after mannitol infusions the patient entered a post-renal failure diuretic phase, following which her urinary function returned to normal for the remainder of her course in the hospital.

In order to evaluate the patient's tolerance to unassisted circulation, the mechanical auxiliary ventricle was turned off on schedule at 7:30 AM on May 20. About 6 hours later the patient's blood pressure fell to 40/30 and the mechanical auxiliary ventricle was turned on with a prompt restoration of blood pressure. On the fifth postoperative day, following an unexplained rise in radial artery pressure to 190/100, the patient developed acute left ventricular failure with pulmonary edema. The mechanical auxiliary ventricle was turned on and the pulmonary edema disappeared within 3–4 minutes. Subsequently the patient remained free of significant hemodynamic prob-

lems. She was alert, sat up with assistance and ate. The patient had several episodes of stupor and paresis on the tenth postoperative day and became comatose following another cerebral vascular accident. She expired on the twelfth postoperative day.

The post-mortem examination showed a thrombus originating at the site of the distal anastomosis, occluding the entire distal limb. There was no thrombus found in the Silastic pumping chamber or in the proximal Dacron graft. The suture lines of the anastomoses were clean and intact. The incision was well healed and there was no apparent infection at the site of entry of the air tube or in its intrathoracic course to the mechanical auxiliary ventricle. The lower lobes of both lungs were boggy. The epicardium showed a fine, fibrinous exudate. There were infarctions of the brain, left kidney and spleen due to thromboemboli. The remainder of the examination was not remarkable.

Discussion

The feasibility of providing long-term assisted circulation had been demonstrated in the experimental studies on dogs performed in our laboratories over a period of 10 years. In the first clinical trial, in February 1966, it was shown that the prosthesis could be successfully implanted and that its operation provided assistance for human failing circulation. The second clinical trial, described here, has confirmed these findings and has provided large amounts of data regarding the hemodynamics of assisted circulation. Several problems developed which required changes in the design characteristics and operation of the mechanical ventricle.

The patient's death was due to thrombosis in the distal limb of the prosthesis which led to fatal thromboembolism. Earlier experimental evidence in the animal studies had demonstrated that clotting in the implanted ventricle could be avoided by complete occlusion of the ascending aorta between the proximal anastomotic site and the brachiocephalic arteries. This diverted all of the blood ejected from the animal's left ventricle through the mechanical ventricle, encouraging copious, continuous washing of the inner surfaces of the prosthesis. As described earlier, in this patient complete occlusion of the aorta was not possible due to elevation in left ventricular pressure when the aorta was clamped. Calculation of the inertial and resistive impedance of a column of blood 30 cm. long retained in the inflexible prosthesis with its long distal limb reveals that this impedance can result in a pressure peak of about 20 mm. Hg. Thus, the rise in pressure upon cross-clamping the aorta was principally due to the great length of the Dacron limbs. This excess length was necessary since the prosthesis did not fit into the planned position in the left chest but had to be implanted in the right hemithorax.

Thus, it was felt that the clotting within the prosthesis resulted indirectly from the failure of the unit to fit in the left hemithorax, requiring long arterial graft segments which introduced so much inertial impedance that the ascending aorta could not be completely closed. The patency of the aorta led, in turn, to a reduced flow of blood through the prosthesis, leading to clot formation.

To eliminate this problem, the shape of the mechanical ventricle has been

Table 1.—*Effect of Mechanical Auxiliary Ventricle on Left Ventricular Pressure Curve in Human (Case 2)*

	MAV Off	MAV On	Difference, %
Area under curve* (sq. cm.)	2.55	1.29	−48
Peak systolic pressure (mm. Hg.)	104	80	−23
End diastolic pressure (mm. Hg.)	30	14	−53
Ejection time (msec.)	160	100	−37

* Area represents time-tension integral.

modified into three new configurations to allow the selection of one which will best fit into the left chest. These models have been tried for fit at many routine post-mortem examinations, including patients who died with congestive heart failure, and good fit has been found in all cases. Thus, in the future the arterial graft segments can be very short; this will allow for reduction in inertial impedance to acceptable levels.

The effects of operation of the auxiliary ventricle on left ventricular pressures are summarized in Table 1. It can be seen that when the mechanical auxiliary ventricle was on there was a reduction of the area under the left ventricular pressure curve of 48 per cent. Thus the mechanical auxiliary ventricle took over nearly half of the ventricular work. This effect resulted in a significant reduction of left ventricular end diastolic pressure.

During the 12 days of operation of the mechanical ventricle there was no evidence of damage to the patient from the implantation or functioning of the prosthesis itself. Technical difficulties prevented the performance of adequate evaluation of renal blood flow. Nonetheless, it is of considerable significance that the patient recovered from an episode of acute renal failure and returned to baseline renal function with the unit operating for 10 more days. The persistent tachycardia noted in the first patient[17] was not present in this second case, so that tachycardia itself does not seem to be related to the prosthesis. An acceptably low amount of hemolysis occurred which is consistent with observations made with artificial heart valves and other fully accepted intravascular prosthetic devices. No infection was introduced by the air pipe leading from the external power supply to the auxiliary ventricle.

The operation of the mechanical assist device prevented the development of left ventricular failure, and on several occasions, relieved acute pulmonary edema which developed during periods when the unit was "off." Arterial blood pressure and central venous pressure were maintained at normal, stable levels by the intermittent use of the mechanical ventricle.

While the experience with these two patients has demonstrated the potential of the mechanical auxiliary ventricle in the treatment of intractable left ventricular failure, more information must be obtained before the device can be used routinely. Our current, in-depth clinical studies are structured to develop data relating to criteria for selection of patients; optimal operational characteristics of the auxiliary ventricle such as pumping cycle, pulse wave

form, stroke volume, and pressures; long-term effects and alterations in physiology of other organs; and principles of management for these patients in all stages of their care.

Summary

1. The implantation of a mechanical auxiliary ventricle is described in two patients, with severe refractory congestive heart failure.

2. The prosthetic device assisted the patient's circulation for a period of 12 days of intermittent operation with no detectable damage.

3. There is evidence that clotting in the prosthesis was a result of excessively long arterial graft segments which can be eliminated due to redesign of the device.

4. The mechanical auxiliary ventricle has reached a stage of development where it can be considered practical for an intensive clinical trial in patients with near terminal congestive heart failure.

5. These trials will define the types of patients who can benefit most from this assist device and will allow the development of standardized surgical techniques and long-term operating criteria for the mechanical auxiliary ventricle.

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